Complete Summary

GUIDELINE TITLE

Pretreatment staging prostate cancer.

BIBLIOGRAPHIC SOURCE(S)

Israel GM, Francis IR, Roach M III, Anscher MS, Bluth EI, Kawashima A, Lee WR, Merrick G, Sandler CM, Fulgham P, Expert Panel on Urologic Imaging and Radiation Oncology-Prostate. Pretreatment staging prostate cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 12 p. [104 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Roach M III, Tempany C, Choyke PL, Anscher MS, Bluth EI, Kawashima A, Lee WR, Sandler CM, Vijayakumar S, Resnick MI, Vijayakumar V, Expert Panel on Radiation Oncology--Prostate Work Group (ROP) and Urologic Imaging. Pretreatment staging prostate cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 11 p. [97 references]

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 23, 2007, Gadolinium-based Contrast Agents: The addition of a boxed warning and new warnings about the risk of nephrogenic systemic fibrosis (NSF) to the full prescribing information for all gadolinium-based contrast agents (GBCAs).

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Prostate cancer

GUIDELINE CATEGORY

Evaluation

CLINICAL SPECIALTY

Nuclear Medicine
Oncology
Radiology
Urology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of initial radiologic examinations for pretreatment staging of patients with prostate cancer

TARGET POPULATION

Patients with prostate cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. X-ray: radiographic survey of the whole body
2. Computed tomography (CT) of the abdomen and pelvis
3. Magnetic resonance imaging (MRI) of the abdomen and pelvis +/- proton spectroscopy

4. Nuclear medicine (NUC)
    - ProstaScint scan
    - Bone scan whole body

MAJOR OUTCOMES CONSIDERED

Accuracy, sensitivity, specificity, and positive and negative predictive value of radiologic procedures for pretreatment staging of prostate cancer

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed to reach agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1 to 9, indicating the most to the least appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Pretreatment Staging Prostate Cancer

Variant 1: T1-2 and GS <6 and PSA <10 and <50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	RRL*
MRI abdomen and pelvis +/- proton spectroscopy	2		None
CT abdomen and pelvis	2		High
NUC ProstaScint scan	2		High
NUC bone scan whole body	2		Med
X-ray radiographic survey whole body	2		Low
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: T1-2 and GS < 6 and PSA <10 and >50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	RRL*
MRI abdomen and pelvis +/- proton spectroscopy	5	Endorectal coil (erMRI) may be considered in patients with high-range PSAs or high-volume disease by biopsy. Useful for treatment planning. See comments regarding contrast in text under "Anticipated Expectations."	None
CT abdomen and pelvis	2		High
NUC ProstaScint scan	2		High
NUC bone scan whole body	2		Med
X-ray radiographic	2		Low

Radiologic Procedure	Rating	Comments	RRL*
survey whole body			
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: T1-2 and GS <6 and PSA 10 to <20 and <50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	RRL*
MRI abdomen and pelvis +/- proton spectroscopy	4	Endorectal coil (erMRI) may be considered in patients with high-range PSAs or high-volume disease by biopsy. Useful for treatment planning. See comments regarding contrast in text under "Anticipated Expectations."	None
NUC bone scan whole body	3	Bone scan may be indicated in patients with PSAs in the high end of this range especially if it is rising rapidly.	Med
CT abdomen and pelvis	2		High
NUC ProstaScint scan	2		High
X-ray radiographic survey whole body	2	If bone scan positive or symptoms dictate.	Low
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: T1-2 and GS <6 and PSA 10 to <20 and >50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	RRL*

Radiologic Procedure	Rating	Comments	RRL*
MRI abdomen and pelvis +/- proton spectroscopy	6	Endorectal coil (erMRI) may be considered in patients with high-range PSAs or high-volume disease by biopsy. Useful for treatment planning. See comments regarding contrast in text under "Anticipated Expectations."	None
NUC bone scan whole body	6	Bone scan should be performed in patients with high-volume disease or PSA in the higher end of this range PSAs especially if it is rising rapidly.	Med
CT abdomen and pelvis	5	CT should be performed in patients with high range PSAs or high volume disease by biopsy. MRI may be substituted.	High
X-ray radiographic survey whole body	5	If bone scan positive or symptoms dictate.	Low
NUC ProstaScint scan	4	Should be reserved for high volume disease.	High
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: T1-2 and GS = 7 and PSA <20 and <50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	RRL*
NUC bone scan whole body	7	Decision to perform bone scan depends on PSA, Gleason (4+3), and volume of disease on biopsy and focality of Gleason 7 tumor. Bone scan should be considered in patients with PSAs in the higher part of this range, especially if it is rising rapidly.	Med
X-ray radiographic survey whole body	6	If bone scan positive or symptoms dictate.	Low
MRI abdomen and pelvis +/- proton spectroscopy	5	Endorectal coil (erMRI) may be considered in patients with high-range PSAs or high-volume disease by	None

Radiologic Procedure	Rating	Comments	RRL*
		biopsy. Useful for treatment planning. See comments regarding contrast in text under "Anticipated Expectations."	
CT abdomen and pelvis	5	CT should be performed in patients with high range PSAs or high volume disease by biopsy. MRI may be substituted.	High
NUC ProstaScint scan	3	If available reserve for high PSA, high volume patients.	High
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: (T1–2 and GS <6 and PSA >20) or T1-2 and GS = 8–10 and PSA <20 and <50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	RRL*
NUC bone scan whole body	8		Med
CT abdomen and pelvis	7	CT should be performed in patients with high range PSAs or high volume disease by biopsy. MRI may be substituted.	High
MRI abdomen and pelvis +/- proton spectroscopy	6	Endorectal coil (erMRI) may be considered in patients with high-range PSAs or high-volume disease by biopsy. Useful for treatment planning. See comments regarding contrast in text under "Anticipated Expectations."	None
X-ray radiographic survey whole body	6	If bone scan positive or symptoms dictate.	Low
NUC ProstaScint scan	5	If available, reserve for high PSA, high volume patients.	High
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: T1-2 and GS >7 and PSA >20 or >50% biopsy cores positive.

Radiologic Procedure	Rating	Comments	RRL*
NUC bone scan whole body	9		Med
MRI abdomen and pelvis +/- proton spectroscopy	8	Endorectal coil (erMRI) may be considered in patients with high-range PSAs or high-volume disease by biopsy. Useful for treatment planning. See comments regarding contrast in text under "Anticipated Expectations."	None
CT abdomen and pelvis	7	MRI may be substituted.	High
X-ray radiographic survey whole body	6	If bone scan positive or symptoms dictate.	Low
NUC ProstaScint scan	5	If available, reserve for high PSA, high volume patients.	High
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 8: Clinical T3, seminal vesicle or bladder neck invasion.

Radiologic Procedure	Rating	Comments	RRL*
NUC bone scan whole body	9		Med
MRI abdomen and pelvis +/- proton spectroscopy	8	Endorectal coil (erMRI) may be considered in patients with high-range PSAs or high-volume disease by biopsy. Useful for treatment planning. See comments regarding contrast in text under "Anticipated Expectations."	None
CT abdomen and pelvis	8	MRI may be substituted.	High

Radiologic Procedure	Rating	Comments	RRL*
X-ray radiographic survey whole body	6	If bone scan positive or symptoms dictate.	Low
NUC ProstaScint scan	5	If available, reserve for high PSA, high volume patients.	High
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Prostate cancer is the most common noncutaneous malignancy of men in the United States and is the second leading cause of cancer death in American men. The American Cancer Society recommends that men over the age of 50 have an annual digital rectal examination (DRE) and a serum prostate-specific antigen (PSA) test, and that men with a family history of prostate cancer or who are of African-American descent begin annual screening at age 45.

If either the DRE or PSA test suggests neoplasm, a transrectal ultrasound-guided needle biopsy of the prostate gland is usually performed. Alternatively, prostate cancer may be found in the tissue obtained during a transurethral resection of the prostate (TURP), although this procedure is becoming less common. Pretreatment staging is important, because clinically localized disease (stage T1 or T2) is generally amenable to local therapy, while more advanced disease may require multimodal therapy (e.g., hormonal ablation and radiation therapy). The TNM system encompasses the status of the primary tumor (T), the lymph nodes (N), and any metastasis (M) (See Appendix 1 in the original guideline document).

Digital Rectal Exam

The DRE, is considered insensitive for detecting extracapsular tumor extension. At least 40% of patients with cancers judged to be clinically confined (T1 or T2) by DRE are found to have extraprostatic extension at surgery. Thus, DRE alone has proven unsatisfactory for determining stage.

Prostate-Specific Antigen

Serum PSA is used as a biomarker, not only in identifying men with prostatic cancer but also in predicting pathologic stage, especially when combined with a patient's Gleason score, and for monitoring treatment response. In general, the higher the PSA, the more advanced the disease; moreover, the likelihood of having organ-confined disease is inversely proportional to the level of the PSA. Despite its utility, it is clear that as many as 15% of men with a normal PSA will have prostate cancer on one or more biopsy specimens. Recent data also suggest

that the correlation with extent of disease is poor for men with relatively low PSA levels (e.g., <9 ng/ml).

The initial PSA value correlates with the likelihood of being free of biochemical evidence of persistent disease and surviving prostate cancer. PSA measurements are evaluated alone or by comparison with a prior measurement [PSA velocity and PSA doubling time (PSADT)], or in the context of the patient's gland volume (PSA density). There are also age-specific PSA levels available. The density and age specificity help to separate the elevations in PSA due to benign prostatic hyperplasia (BPH) from those due to cancer; however, these methods provide guidance only on the likelihood of cancer versus benign disease. The capability of PSA level alone to accurately predict final pathologic stage in an individual has a prohibitively high false positive rate. Recently, the bound and free components of PSA have been measured; the proportion of free PSA (ie, not bound to plasma proteins) was lower in patients with cancer than in those with BPH. For instance, free PSA values <15% were associated with more aggressive tumors, whereas free PSA values >25% generally had low-risk tumors.

Prostate Acid Phosphatase

With the introduction of PSA in the 1980s, prostate acid phosphatase (PAP) fell into disfavor because PSA performed significantly better in terms of screening and monitoring response to treatment. However, recent radical prostatectomy, external-beam radiation therapy, and brachytherapy series have demonstrated that PAP is a statistically significant predictor for biochemical progression-free survival and/or cause-specific survival in patients with intermediate- and high-risk prostate cancer. PAP appears to be particularly valuable in predicting distant failure in higher-risk patients for whom high levels of local control are achieved with aggressive local treatment. If PAP is to be introduced as a standard component of the initial diagnostic workup of prostate cancer, additional clinical studies are necessary to corroborate the currently published data.

Gleason Score

The Gleason scoring system has been shown to correlate well with the extent of disease and prognosis. It is the single best predictor of the biological activity, and therefore the stage, of the tumor. The scoring ranges from 2 (well differentiated, minimally aggressive) to 10 (anaplastic, highly malignant). The probability of seminal vesicle and lymph node involvement increases with the Gleason score, and some investigators have found a combination of the Gleason score and serum PSA level to give the greatest prognostic information.

Nomograms and Risk Group Stratification

The work by one group of investigators has led to the development of nomograms that predict the probability of extracapsular extension (ECE), seminal vesicle involvement (SV+), and lymph node involvement (LN+). This work was subsequently validated by others and led to attempts to correlate nomograms with prognosis. Most nomograms use combinations of clinically available prognostic factors such as PSA level, grade, and clinical T stage to estimate the risk. Estimates of the probability of LN positivity derived from such nomograms

have subsequently been shown to be of use in determining the utility of staging studies and in guiding therapy.

Clinicians have widely adopted a simplified approach to predicting outcome based on the same pretreatment parameters used in the nomograms. Using such an approach, patients with similar risk of biochemical recurrence can be divided into risk groups that, with additional follow-up, have been correlated with mortality:

Low Risk	2002 AJCC clinical stage T1c, 2a and PSA ≤10 ng/ml and biopsy Gleason score ≤6%~80% 10-year PSA failure-free survival rate.
Intermediate Risk	2002 AJCC clinical stage T2b or PSA >10 and ≤20 ng/ml or biopsy Gleason score 7%~50% 10-year PSA failure-free survival rate.
High Risk	2002 AJCC stage T2c disease or PSA >20 ng/ml or biopsy Gleason score ≥8%~33% 10-year PSA failure-free survival rate.

Alternative risk stratification schemes have also been described, but despite their differences they support the notion that Gleason score, clinical T stage, and PSA can be used to predict survival and direct therapy. More recently the number of positive biopsies (e.g., >5) and the percentage of each core that is positive for biopsy (e.g., >50%) have been associated with increased risk of recurrent disease.

Summary of Nonimaging Methods of Staging

While digital rectal examination, PSA test, or Gleason score individually predict stage, they are less accurate than when they are combined into nomograms that provide estimates of risk. Patients can be stratified by their risk for extraprostatic, nodal, and disseminated disease.

Imaging potentially improves these general estimates of risk by specifically identifying lesions with anatomic abnormalities. However, interpretation of imaging findings should be made in the context of the nonimaging findings. Due in part to the limitations of clinical staging, efforts have been made to use imaging modalities to better predict the extent of disease and outcome.

Imaging Methods

Ultrasound

Gray-scale ultrasound (US) has not proven satisfactory for local staging of prostate cancer. The ability of transrectal US to predict extracapsular extension varies widely from 37%–83% in different settings and populations; however, it is generally acknowledged that US is of limited value due to limitations of its spatial resolution. The addition of color Doppler and power Doppler improves the detection of prostate cancer by identifying increased vascularity but has not yet been shown to improve staging accuracy. Failure to identify a neurovascular bundle near the site of a tumor is suggestive of extracapsular extension, but there is not yet consensus that its use is mandatory for staging. Contrast-enhanced US has the potential to substantially improve the staging of prostate cancer but has not yet been tested in a multi-institutional trial. Similarly 3D US is under investigation to improve the delineation of the cancer and prostate capsule.

Magnetic Resonance Imaging

Endorectal coil magnetic resonance imaging (erMRI) provides the highest spatial resolution among the imaging modalities currently available. Three major techniques that have been used to stage prostate cancer with erMRI: T2-weighted MRI, MR spectroscopic imaging (MRSI), and dynamic contrast-enhanced MRI (DCE-MRI). It is generally accepted that an endorectal coil is required to achieve sufficient signal-to-noise ratios to allow small field-of-view (12–16 cm) imaging which, in turn, allows images to be acquired with high resolution (~0.5 mm). Additionally, 3-Tesla (3T) erMRI may be beneficial by providing higher signal, thus further improving spatial (or temporal, in the case of DCE-MRI) resolution. One group of researchers have shown that 3T erMRI imaging is accurate for staging of prostate cancer, that there is moderate to substantial interobserver agreement, and that minimal capsular invasion could be detected. However, there are insufficient data in the literature to support the routine use of 3T erMRI.

T2-Weighted MRI

Over 15 years of clinical experience exists with T2- weighted erMRI. Improvements in coil design (dual endorectal coil and torso coil arrays), pulse sequences, and image correction have led to improvements in the performance of T2-weighted imaging, but some inherent limitations remain. Low-signal lesions on T2-weighted imaging can be due to cancer or can be caused by benign processes such as prostatitis. Endorectal coil MRI remains limited in its ability to identify microscopic or early macroscopic capsular penetration due to restrictions on spatial resolution and motion artifacts. Moreover, individual radiologist expertise is an important determinant of staging accuracy. In one study, one reader achieved an accuracy of 91%, while the other had an accuracy of only 56%.

Early studies from the 1990s reported accuracies from 51%-82% in distinguishing T2 and T3 disease. More recently, erMRI has been shown to improve the prediction of neurovascular bundle invasion prior to radical prostatectomy. One study demonstrated that the differences between "expert" readers and less experienced readers could be reduced by incorporating other clinical data (e.g., PSA value, tumor grade) and using strict imaging criteria. Another study showed that using dynamic contrast-enhanced MRI rather than T2-weighted images can improve staging performance by less experienced readers, when compared to more experienced readers. Endorectal MRI has also been shown to be accurate in demonstrating seminal vesicle invasion. The combination of a tumor at the base of the prostate that extends beyond the capsule combined with low signal in the seminal vesicles that have lost normal architecture is highly predictive of seminal vesicle invasion.

More recently, similar strategies to include erMRI in a neural network have resulted in overall accuracies of 88% to 91% depending on the exact implementation. These results are superior to conventional results with Partin's tables. In this study, Gleason score was the most influential predictive factor, followed by erMRI results and then PSA levels. Several studies have documented that erMRI is most successful in men with intermediate-risk prostate cancer based on Partin's tables. In these men, erMRI staging was highly predictive of PSA recurrence. In a study involving 344 patients, one group of investigators demonstrated that erMRI added statistically meaningful staging data regarding

extracapsular extension. Endorectal MRI has also proven helpful in directing 3D conformal radiotherapy and improving outcomes.

MR Spectroscopy

One group of investigators have demonstrated that prostate cancers have a characteristic loss of the citrate peak and gain in the choline/creatine peak on MR spectroscopic imaging. Moreover, the ratio of choline to citrate is related to the Gleason score, suggesting that MRSI may provide information about tumor aggressiveness. Improvements in diagnostic accuracy and staging have been reported. However, MRSI is technically demanding and time consuming. It has not been proven in multi-institutional trials, although a clinical trial under the auspices of the American College of Radiology Imaging Network (ACRIN®) is currently underway. Thus, MRSI cannot yet be considered a routine diagnostic tool.

Dynamic Contrast-Enhanced MRI

Prostate cancers, like many tumors, demonstrate angiogenesis that can be detected on dynamic contrast-enhanced MRI (DCE-MRI). DCE-MRI demonstrates earlier and more intense enhancement in sites of tumor. One group of investigators found minimal improvements in diagnostic accuracy over conventional T2-weighted scans using DCE-MRI. Another group showed that tumors could be distinguished from noncancerous prostate with high reliability, although the study did not specifically address staging. It has also been shown that DCE-MRI can improve staging performance when used in conjunction with T2-weighted images for less experienced readers when compared to more experienced readers. However, this method still suffers from a lack of a uniformly accepted analytic method and has not been tested in multi-institutional trials. Thus, it is still of unproven benefit.

Nodal Staging with MRI

MRI has been shown to be at least equivalent to computed tomography (CT) for detecting abnormal lymph nodes in men with prostate cancer. Neither MRI nor CT scans are as accurate as laparoscopic node dissection. Unfortunately, metastatic lymph nodes in prostate cancer are often small, so that conventional size criteria underestimate the extent of nodal disease. Thus, low sensitivities are observed, even in high-risk patients. Ultrasmall particles of iron oxide (USPIO) have been shown to dramatically improve sensitivity of MRI for nodal metastasis; however, the iron-based contrast agent ferumoxytran (trade name Combidex) is not yet approved by the FDA. The role of MRI for nodal staging will need to be reassessed if the FDA approves Combidex.

Computed Tomography

CT of the abdomen and pelvis is occasionally used to preoperatively stage prostate cancer, but its staging accuracy is usually considered poor. CT scans have suffered from poor sensitivity in detecting capsular penetration, seminal vesicle involvement, and lymph node extension and should be reserved for use in patients with a high probability of lymph node involvement. Overall accuracy in staging was reported as 65% by one group of investigators and as 67% by another group. For loco-regional staging, such as extracapsular penetration, the

accuracy has been reported as low as 24%. Even with refined techniques in performing CT (3 mm slice thickness and 5 mm table increments with both IV and oral contrast), it has been concluded that CT is of little value in staging the local extent of prostatic carcinoma. However, one study reports 93.7% accuracy for CT in detecting positive lymph nodes, which increases to 96.5% if CT-guided fine-needle aspiration biopsy is added. This degree of accuracy was only achieved by using a threshold of 6 mm or larger as pathologic. Thus, CT of the abdomen and pelvis is of limited value in local staging and nodal staging and should be reserved for intermediate- and high-risk patients.

ProstaScint (Indium Capromab)

The reliability and usefulness of ProstaScint scan based on indium-111 radiolabeled capromab pendetide (a first-generation monoclonal antibody against prostate-specific membrane antigen [PSMA]) as a method to help initial staging in prostate cancer remain unproven at this time. Initial studies suggested that this technology may improve the detection of metastatic lymph nodes when applied to patients estimated to have a risk of lymph node involvement of >20%. Studies are needed with a sufficient number of patients with histopathological correlation to document sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. One group of investigators conducted histopathological correlation in lymph nodes after ProstaScint scan in 31 patients (43 samples). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy value were 94%, 42%, 53%, 92%, and 65%, respectively. Its limitations appear to be due to the intracellular binding site of the antibody as well as nonprostatic expression of PSMA. Routine ProstaScint scanning as an initial staging procedure is not justified based on evidence at this time. However, many studies show its utility in postoperative failure settings, especially to guide radio therapeutic decisions. New methods to suppress normal uptake as well as coregistration and fusion with CT or MRI seem to improve its utility in defining target volumes in radio therapeutic settings.

Bone Scan

The radionuclide bone scan is a standard component of the evaluation for many patients diagnosed with prostate cancer. However, original work by one group of investigators has shown that in patients with low PSA level (<10 ng/mL) who have no pain, the yield of a staging bone scan is too low to warrant its routine use. In their experience, no patient with a PSA ≤ 10/ng/mL had a positive bone scan, and only one patient in 300 with a PSA level ≥20 ng/mL had a positive radionuclide bone scan. Such observations have been confirmed by more recent studies as well. These studies suggest that for patients with no skeletal symptoms and a serum PSA level of 10 ng/mL or less, a staging radionuclide bone scan is not necessary; however, this recommendation has to be modified under specific circumstances such as T3 or T4 disease or a high Gleason score.

The rate of positive bone scans depends on the PSA value and Gleason score. Patients with PSA ≤20 ng/mL and Gleason Score <8 have a 1% to 13% rate of positive bone scans. For this reason patients with a PSA ≥20 ng/mL (with any T stage or Gleason score), locally advanced disease (T3 or T4 with any PSA or Gleason score), or Gleason score of 8 or greater (with any PSA or T stage) should

be considered for a radionuclide bone scan. Patients with skeletal symptoms or advanced stage disease should also be considered candidates for bone scans.

Positron Emission Tomography

The role of positron emission tomography (PET) in the staging workup of newly diagnosed and recurrent prostate cancers is still being evaluated. It has the potential to play an important role in detecting early metastatic spread and monitoring post-therapy response. The most commonly available PET tracer, FDG-PET, has proven disappointing in the initial staging of prostate cancer. In that study 23 of 24 primary prostate cancer lesions were not detected by FDG-PET. FDG-PET can play a role in the detection of local recurrence and/or distant metastases with increasing PSA after initial treatment failure. Several additional radiotracers have been extensively studied, including C11 or F18 choline and acetate, C11 methionine, F18 fluoride, and fluorodihydrotestosterone. PET scans using these radiotracers may help in the clinical decision-making process, especially in patients with high-risk primary disease, but these agents are not yet widely available. For instance, in the detection of nodal metastases, C11 choline or acetate PET appears to be promising.

New agents such as fluorodihydrotestosterone and gallium-68-labeled peptides are being studied, and these approaches using small chelator-coupled peptides can have advantages over other traditional agents. These tracers remain experimental. Thus, PET scanning has a limited role in the staging of prostate cancer.

Chest Radiography

There are no data in the literature documenting the yield of a chest x-ray. Therefore, it should be performed as part of the initial staging only with suspected metastatic disease (e.g., PSA >100 ng/mL) or in patients who are heavy smokers with clinically localized disease.

Summary

In summary, the guidelines for pretreatment staging of prostate cancer should be individualized based on consideration of the clinical parameters that are predictive of the likelihood of ECE, SV+ and LN+. These clinical parameters should include: the pretreatment PSA level and the rate of rise or doubling time, the Gleason score, the palpation T stage, the number of positive biopsies, and the percentage of the specimen involved.

The role of imaging in low-risk patients is controversial. In intermediate- and high-risk individuals, imaging may play a role in staging and thus in directing therapy. MRI using endorectal coil techniques appears to be the most accurate imaging test available for local staging of the prostate, providing both loco-regional and nodal evaluation. The accuracy of the technique appears related to the experience of the radiologists. MR spectroscopy and dynamic contrast-enhanced MRI may be useful adjuncts in the future but are, as yet, unproven in multiinstitutional trials.

In truly high-risk patients (clinical T3, very high PSA levels, and Gleason score ≥8), radionuclide bone scans and CT may be useful for detecting bony metastases and lymph nodes, respectively. ProstaScint scans may also play a role in detecting nodal metastases in selected high-risk patients, but the modest accuracy of this test has led most experts to consider its value dubious. PET scans with FDG are of limited value in initial staging but may be more useful in recurrent and metastatic disease.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF, also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors and lay people. Until the last few years, gadolinium-based MR contrast agents were widely believed to be almost universally well tolerated, extremely safe and non-nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF, a syndrome that can be fatal. Further studies are necessary to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function and NSF. Current theory links the development of NSF to the administration of relatively high doses (e.g.,>0.2 mM/kg) and to agents in which the gadolinium is least strongly chelated. The FDA has recently issued a "black box" warning concerning these contrast agents (http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705HCP.pdf).

This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m^2), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

Abbreviations

- CT, computed tomography
- erMRI, endorectal coil magnetic resonance imaging
- GS, Gleason score
- Med, medium
- MRI, magnetic resonance imaging
- NUC, nuclear medicine
- PSA, prostate-specific antigen
- T, tumor

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate selection of radiologic imaging procedures for pretreatment staging of patients with prostate cancer

POTENTIAL HARMS

- The relative radiation level is high for computed tomography (CT) of the abdomen and pelvis and nuclear medicine (NUC) ProstaScint scan; medium for NUC bone scan of the whole body; and low for X-ray radiographic survey of the whole body.
- Some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed nephrogenic systemic fibrosis, a syndrome that can be fatal. Until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made

by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Israel GM, Francis IR, Roach M III, Anscher MS, Bluth EI, Kawashima A, Lee WR, Merrick G, Sandler CM, Fulgham P, Expert Panel on Urologic Imaging and Radiation Oncology-Prostate. Pretreatment staging prostate cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 12 p. [104 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1995 (revised 2007)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panels on Radiation Oncology-Prostate Work Group (ROP) and Urologic Imaging (URI)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Gary M. Israel, MD; Isaac R. Francis, MD; Mack Roach III, MD; Mitchell S, Anscher, MD; Edward I. Bluth, MD; Akira Kawashima, MD, PhD; William R. Lee, MD; Gregory Merrick, MD; Carl M. Sandler, MD; Pat Fulgham, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Roach M III, Tempany C, Choyke PL, Anscher MS, Bluth EI, Kawashima A, Lee WR, Sandler CM, Vijayakumar S, Resnick MI, Vijayakumar V, Expert Panel on Radiation Oncology--Prostate Work Group (ROP) and Urologic Imaging. Pretreatment staging prostate cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 11 p. [97 references]

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Relative radiation level information. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on November 15, 2004. The information was verified by the guideline developer on December 21, 2004. This summary was updated by ECRI on March 23, 2006. This NGC summary was updated by ECRI Institute on December 4, 2007.

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DISCLAIMER

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